CLAIMS

1. A water-soluble reference standard for an immunoassay of a lipophilic drug, of formula (I):

$G–(L)_n–Y$ (I);

wherein

G is a lipophilic drug;

L is a linker selected from the group consisting of alkyl and heteroalkyl containing from 1 to 20 carbon atoms;

n is 0 or 1; and

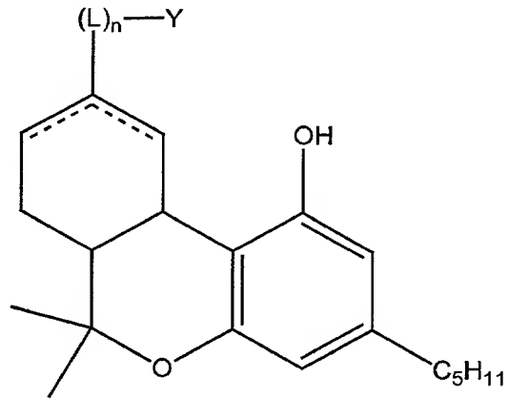
Y is a water-solubilizing group selected from the group consisting of $–SO_3^-$, $–NR-SO_3^-$, $–P(=O)(OH)(O^-)$, or $–O-P(=O)(OH)(O^-)$;

wherein R is selected from the group consisting of H and an alkyl group comprising 1 to 10 carbon atoms.

2. The water-soluble reference standard of claim 1, wherein G is selected from the group consisting of benzodiazepines, cannabinoids, opiates, cocaine, propoxyphene, phencyclidines, methaqualone, barbiturates, LSD, amphetamines, tricyclic antidepressants, and methadone.

3. The water-soluble reference standard of claim 1, wherein Y is $–NR-SO_3^-$.

4. The water-soluble reference standard of claim 1, wherein $G–(L)_n–Y$ is a compound of formula (V)



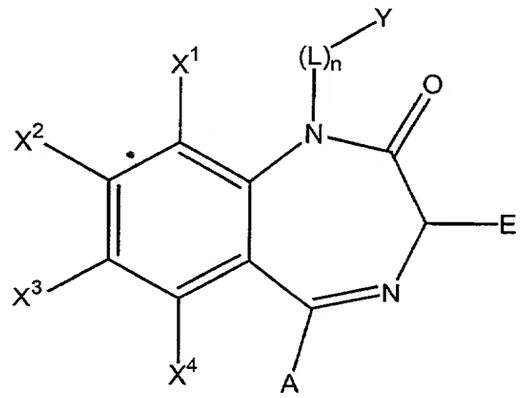
(V).

5. The water-soluble reference standard of claim 4, wherein n is 0 and Y is $-NH-SO_3^-$.

6. The water-soluble reference standard of claim 4, wherein n is 1; L is $-CH_2-$; and Y is $-NH-SO_3^-$.

7. The water-soluble reference standard of claim 1, wherein G is a benzodiazepine.

8. The water-soluble reference standard of claim 1, wherein G–$(L)_n$–Y is a compound of formula (II)



(II);

wherein X^1, X^2, X^3 and X^4 are independently selected from the group consisting of hydrogen, F, Cl, Br, nitro, amino, and alkylamido;

-L- is an alkyl or heteroalkyl group containing from 1-20 carbon atoms;

-E is -H, alkyl, -OH, -COOH, or –COOR', where R' is an alkyl group containing from 1 to 10 carbon atoms; and

A is an aryl group.

9. The water-soluble reference standard of claim 8, wherein

L is $-CH_2CH_2-$;

n is 1; and

Y is $-NHSO_3^-$.

10. The water-soluble reference standard of claim 9, wherein

X^1, X^2, and X^4 are hydrogen;

X^3 is Cl; and

A is 2-fluorophenyl.

11. The water-soluble reference standard of claim 1, wherein the compound has a solubility of at least 100 micrograms per milliliter in water at 25°C.

12. The water-soluble reference standard of claim 1, wherein the compound has a solubility of at least 500 micrograms per milliliter in water at 25°C.

13. The water-soluble reference standard of claim 1, wherein the compound has a solubility of at least 1 milligram per milliliter in water at 25°C.

14. The water-soluble reference standard of claim 1, wherein the compound has an octanol/water partition coefficient which is constant within a pH of 2 to 14.

15. The water-soluble reference standard of claim 1, wherein the compound has an octanol/water partition coefficient which is constant within a pH of 3 to 12.

16. The water-soluble reference standard of claim 1, wherein the compound has an octanol/water partition coefficient which is constant within a pH of 5 to 9.

17. The water-soluble reference standard of claim 1, wherein the compound, when dissolved in an aqueous mixture at an initial concentration, retains at least 50% of the initial concentration at a temperature of 45°C for 14 days.

18. The water-soluble reference standard of claim 1, wherein the compound, when dissolved in an aqueous mixture at an initial concentration, retains at least 75% of the initial concentration at a temperature of 45°C for 14 days.

19. The water-soluble reference standard of claim 1, wherein the compound, when dissolved in an aqueous mixture at an initial concentration, retains at least 90% of the initial concentration at a temperature of 45°C for 14 days.

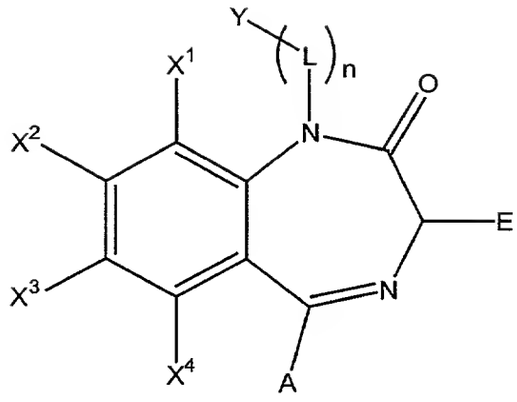
20. The water-soluble reference standard of claim 1, wherein the compound, when dissolved in an aqueous mixture at an initial concentration, retains at least 93% of the initial concentration at a temperature of 45°C for 14 days.

21. The water-soluble reference standard of claim 1, wherein the compound, when dissolved at an initial concentration in an aqueous mixture having a pH from 2 to 13, retains at least 50% of the initial concentration at a temperature of 45°C for 14 days.

22. The water-soluble reference standard of claim 1, wherein the compound, when dissolved at an initial concentration in an aqueous mixture having a pH from 5 to 9, retains at least 50% of the initial concentration at a temperature of 45°C for 14 days.

23. The water-soluble reference standard of claim 1, wherein the compound, when dissolved at an initial concentration in an aqueous mixture having a pH from 6 to 8, retains at least 50% of the initial concentration at a temperature of 45°C for 14 days.

24. A water-soluble reference standard for an immunoassay of benzodiazepines, of formula (II):



(II);

wherein X^1, X^2, X^3 and X^4 are independently selected from the group consisting of hydrogen, F, Cl, Br, nitro, amino, and alkylamido;

E is selected from the group consisting of -H, alkyl, -OH, -COOH, and –COOR', where R' is an alkyl group containing from 1 to 10 carbon atoms;

A is an aryl group

L is a linker group selected from the group consisting of alkyl and heteroalkyl containing from 1-20 carbon atoms;

n is 0 or 1; and

Y is selected from the group consisting of $–SO_3^-$, $–NR'-SO_3^-$, $–P(=O)(OH)(O^-)$, or $–O-P(=O)(OH)(O^-)$;

wherein R' is selected from the group consisting of H and an alkyl group comprising 1 to 10 carbon atoms;

wherein the compound has a solubility of at least 100 micrograms per milliliter in water at 25°C.

25. The water-soluble reference standard of claim 24, wherein

L is $–CH_2CH_2-$;

n is 1; and

Y is $-NHSO_3^-$.

26. The water-soluble reference standard of claim 25, wherein

X^1, X^2, and X^4 are hydrogen;

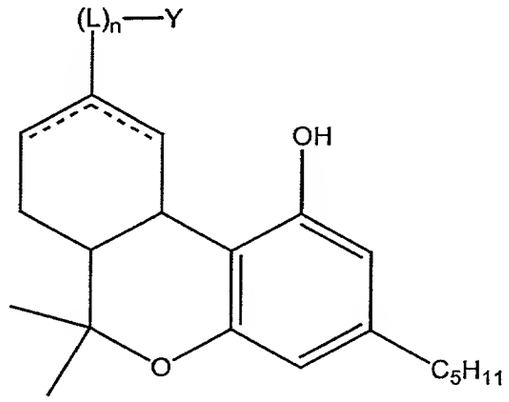
X^3 is Cl; and

A is 2-fluorophenyl.

27. The water-soluble reference standard of claim 24, wherein the compound, when dissolved in an aqueous mixture at an initial concentration, retains at least 50% of the initial concentration at a temperature of 45°C for 14 days.

28. The water-soluble reference standard of claim 24, wherein the compound, when dissolved at an initial concentration in an aqueous mixture having a pH from 2 to 13, retains at least 50% of the initial concentration at a temperature of 45°C for 14 days.

29. A water-soluble reference standard for an immunoassay of THC, of formula (V):



(V);

wherein L is a selected from the group consisting of alkyl and heteroalkyl containing from 1 to 20 carbon atoms;

n is 0 or 1; and

Y is selected from the group consisting of $-SO_3^-$, $-NR'-SO_3^-$, $-P(=O)(OH)(O^-)$, or $-O-P(=O)(OH)(O^-)$;

wherein R' is selected from the group consisting of H and an alkyl group comprising 1 to 10 carbon atoms; and

wherein the compound has a solubility of at least 100 micrograms per milliliter in water at 25°C.

30. The water-soluble reference standard of claim 29, wherein n is 0 and Y is $-NH-SO_3^-$.

31. The water-soluble reference standard of claim 29, wherein n is 1; L is $-CH_2-$; and Y is $-NH-SO_3^-$.

32. A method of forming a water-soluble reference standard for immunoassay of a lipophilic drug, comprising:

functionalizing a lipophilic drug with a water-solubilizing group selected from the group consisting of $-SO_3^-$, $-NR'-SO_3^-$, $-P(=O)(OH)(O^-)$, or $-O-P(=O)(OH)(O^-)$.

33. The method of claim 32, further comprising modifying the lipophilic drug with a linking group.

34. The method of claim 32, wherein the functionalizing comprises treating the liphophilic drug with chlorosulfonic acid.

35. The method of claim 32, wherein the functionalizing comprises treating the liphophilic drug with sulfuric acid.

36. A method of forming a water soluble reference standard for an immunoassay of THC, comprising:

reacting THC-9-carboxylic acid with DPPA and sodium hydroxide to form THC-9-amine; and

treating THC-9-amine with chlorosulfonic acid.

37. A method of forming a water soluble reference standard for an immunoassay of THC, comprising:

treating THC-9-carboxylic acid with DCC and NHS to form an ester;

treating the ester with ammonium hydroxide to form THC-9-amide;

reducing the THC-9-amide with lithium aluminum hydride to form THC-9-amine; and

reacting the THC-9-amine with chlorosulfonic acid.

38. A method of forming water soluble reference standard for an immunoassay of benzodiazepines, comprising:

treating didesethylflurazepam with chlorosulfonic acid.

39. An assay method for dètermining a lipophilic drug, comprising:

combining a first sample containing the reference standard of claim 1 with the reagent, the reagent capable of forming a first detectable complex with said reference standard;

determining the presence or amount of said first detectable complex in said sample;

combining a second sample suspected of containing said drug with a reagent comprising the antibody of said drug, and the reagent capable of forming a second detectable complex with said drug;

determining the presence or amount of said second detectable complex in said sample; and

comparing the presence or amount of said first detectable complex with the presence or amount of said second detectable complex as a measure of said drug in said sample.

40. An assay method for determining benzodiazepines, comprising:

combining a first sample containing the reference standard of claim 24 with the reagent, the reagent capable of forming a first detectable complex with said reference standard;

determining the presence or amount of said first detectable complex in said sample;

combining a second sample suspected of containing said drug with a reagent comprising the antibody of said drug, and the reagent capable of forming a second detectable complex with said drug;

determining the presence or amount of said second detectable complex in said sample; and

comparing the presence or amount of said first detectable complex with the presence or amount of said second detectable complex as a measure of said drug in said sample.

41. An assay method for determining THC, comprising:

combining a first sample containing the reference standard of claim 29 with the reagent, the reagent capable of forming a first detectable complex with said reference standard;

determining the presence or amount of said first detectable complex in said sample;

combining a second sample suspected of containing said drug with a reagent comprising the antibody of said drug, and the reagent capable of forming a second detectable complex with said drug;

determining the presence or amount of said second detectable complex in said sample; and

comparing the presence or amount of said first detectable complex with the presence or amount of said second detectable complex as a measure of said drug in said sample.

42. A reference standard kit, comprising the reference standard of claim 1.

43. A reference standard kit, comprising the reference standard of claim 24.

44. A reference standard kit, comprising the reference standard of claim 29.